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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/088,699 | 06/14/2002 | Ikuo Nishimoto | 082376-000000US | 2315 |

7590 03/02/2007

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| EXAMINER | |
|---|---|
| SCHLAPKOHL, WALTER | |
| ART UNIT | PAPER NUMBER |
| 1636 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 03/02/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/088,699 | NISHIMOTO, IKUO | |
| | Examiner | Art Unit | |
| | Walter Schlapkohl | 1636 | wal |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2-4,6,8-10,12 and 18-21* is/are pending in the application.

4a) Of the above claim(s) *3 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,6,8,10,12 and 18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Receipt is acknowledged of the papers filed 12/12/2006 in which claims 2, 4, 6, 8, 10 and 12 were amended, and claims 5, 7, 11, and 13-17 were canceled. Claims 2-4, 6, 8-10, 12 and 18-21 are pending. Claims 3 and 9 are withdrawn. Claims 2, 4, 6, 8, 10, 12, and 18-21 are under examination in the instant Office action.

Any rejection of record, not recited herein, is hereby withdrawn.

### *Claim Objections*

The claim objection to claim 2 is withdrawn in view of Applicant's amendment to the claim.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 8 & 10, and therefore dependent claims 19 & 21, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly

claim the subject matter which Applicant regards as the invention. **These are new rejections necessitated by Applicant's amendment(s).**

Claim 4 recites "[t]he method according to claim 2, comprising the step of inducing the cell death associated with said disorder before, during or after step (a), and wherein the suppressive effect on the disorder in step (b) is a suppression of cell death" in lines 1-4 (emphasis added). Claim 4 is vague and indefinite because it is not clear how cell death can be induced *before* the suppression of cell death is detected. Does Applicant intend a method wherein cell death is induced, but delayed until after the suppression of cell death has been determined, or does Applicant intend such a method wherein cell death is induced in only some cells or in cells in the vicinity of those cells in which the cell death is induced and said suppressive effect is determined by suppressed cell death in the remaining live cells or the cells in the vicinity of the area of cell death?

Similarly, claim 10 recites "[t]he method according to claim 8, comprising the step of inducing the cell death associated with said disorder before, during or after step (a), and wherein the suppressive effect on the disorder in the step (b) is a suppression of cell death" in lines 1-4 (emphasis

added). Claim 10 is vague and indefinite as explained for claim 4, above.

Claim 8 recites "[a] method for testing a suppressive effect of a nucleic acid on a neurodegenerative disorder of a cranial nervous system, wherein said method comprises the steps of:

(a) expressing in a population of cells a library of nucleic acids obtained from or synthesized from a nucleic acids expressed in a tissue of a nerve or brain of an organism suffering from the neurodegenerative disorder of a cranial nervous system, wherein said tissue is obtained from an area showing cell death as a pathological feature of the disorder, and,

(b) detecting the suppressive effect on the disorder due to the expression of the a nucleic acid of the library; thereby identifying a suppressive effect of a nucleic acid on the disorder" in lines 1-11 (emphasis added). Claim 8 is vague and indefinite in that the metes and bounds of a "tissue of a nerve" are unclear. Does Applicant intend any tissue in which a nerve cell is found, or does Applicant intend, e.g., the use of a single nerve cell?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 4, 6, 8, 10, 12 and 18-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons of record.**

*Response to Arguments*

Applicant asserts that the present invention is based, at least in part, on the inventive insight into a "general phenomenon" that surviving cells from, or in the vicinity of, affected tissues of a disorder accompanying cell death sufficiently express disorder suppressor genes that prevent the development of pathological symptoms, and further that a condensed library of disorder suppressor genes can be prepared from such tissues for identifying disorder suppressor genes.

Applicant further asserts that this insight had not been previously described in the art (see page 9, 1st paragraph of the Remarks filed 12/12/2006; emphasis added). Applicant submits that written descriptive support for the present invention should be determined in the context of Applicant's insight as summarized in Applicant's remarks (ibid, especially page 9, lines 13-15; emphasis added).

Applicant further argues that, to the extent that the Examiner may be suggesting that written description for the present claims requires description of particular sequences having a suppressive effect on a disorder, Applicant disagrees and asserts that *a priori* knowledge of the structure or function of a particular disorder suppressor gene to be identified is not necessary.

Applicant further argues that the claims have been amended to expedite prosecution and that, in view of the amendments, "any alleged bases for rejection that pertain to disorders other than a neurodegenerative disorder of a cranial nervous system, or nucleic acids other than those derived from a tissue of a nerve or brain are obviated" (see page 10, 1st paragraph).

Applicant further argues that the underlying inquiry in determining compliance with the written description requirement is "whether the specification describes the claimed invention in

sufficient detail that one of skill in the art can reasonably conclude that the inventor had possession of the claimed invention" (see page 10, 1st full paragraph). Applicant further argues that possession of the claimed invention can be shown in any number of ways and that any assessment of written description in the instant case must include the recognition that 1) diseases involving cell death, including affected organs and tissues, were generally known as of the filing date; 2) neurodegenerative disorders, the affected tissues in such diseases and their characteristic clinical symptoms were also known in the art; and 3) procedures for making an expression library from a tissue sample were also well-known in the art at the time of Applicant's filing (see page 11, last full paragraph and paragraph bridging pages 11 and 12 of the Remarks filed 12/12/06).

Applicant also argues that because the recited nucleic acids of the claims are clearly defined in terms of the process of obtaining them, functional or structural characteristics of such nucleic acids are not necessary to satisfy the written description requirement.

Applicant further argues that Examiner has asserted that the claims are "process claims with a product-by-process claim embedded in them" (see page 12, 1st full paragraph of the Remarks

filed 12/12/06). Applicant further notes that the MPEP states that the disclosure of only a method of making the invention and the function of the product may be sufficient to support a product-by-process claim (MPEP § 2163 (II)(A)(3)(a)(i). As such, Applicant argues, because one of ordinary skill in the art could carry out the process to obtain the nucleic acid library as recited in the claims, as well as a population of cells expressing the library, one of ordinary skill in the art would readily accept Applicant's possession of these features.

Applicant further argues that actual reduction to practice is not required to satisfy the written description requirement and that Applicant has provided not one, but two working examples of cell types and, further that Applicant's invention yielded not one, but 36 non-overlapped clones as examples of nucleic acids obtained by such a method.

With regard to other disorders for which the claimed method can be practiced, Applicant argues that 1) such disorders are listed in the specification; and 2) it was well-accepted in the art that virtually all disorders are caused by a collapse in the balance between the action of disease-causing aberrant genes and that it is "highly likely" that suppressor genes for a majority of disorders are present in the genome (see page 14, 1st paragraph and page 15, 1st full paragraph of the Remarks filed

12/12/06). Applicant further argues that such knowledge, combined with Applicant's insight that surviving cells from affected areas will express disorder suppressor genes with increased frequency, as well as Applicant's "proof of principle" comprising the identification of a single disorder suppressor gene from tissue obtained from the brain of an Alzheimer's patient would lead the skilled artisan to ready accept that the claimed method has "general applicability" and thus reasonably conclude that Applicant had possession of the invention as claimed.

Finally, Applicant argues that no evidence has been provided that would tend to refute the specification's disclosure or the knowledge in the art as summarized in Applicant's instant remarks.

Applicant's arguments have been carefully considered but have respectfully been found unpersuasive. To begin, Examiner agrees with Applicant's assertion that *a priori* knowledge of the structure or function of a particular disorder suppressor gene to be identified is not necessary. Examiner further acknowledges that Applicant's amendments have addressed some of the considerations recited in the written description rejection set forth in the Office action mailed 7/11/2006. Examiner

further agrees with Applicant insofar as possession is the underlying inquiry of the written description rejection of claims under 35 U.S.C. 112, 1st paragraph. Examiner also agrees with Applicant insofar as possession of the claimed invention can be demonstrated in a variety of ways and that actual reduction to practice is not a requirement for demonstration of possession of the claimed invention.

However, Applicant's assertion that the present invention is based, at least in part, on the inventive insight into "a general phenomenon" that surviving cells from, or in the vicinity of, affected tissues of a disorder accompanying cell death sufficiently express disorder suppressor genes that prevent the development of pathological symptoms, and further that a condensed library of said disorder suppressor genes can be prepared from such tissues for identifying disorder suppressor genes stands in high contrast to Applicant's assertion in the specification that "[i]n disorders that accompany cell death, a pathological feature is the degeneration of cells in affected areas of organs or tissues in which cell death occurs. Usually, such disease organs and tissues may not be suitable objects for screening for a disorder suppressor gene, even though they can be objects for screening for a disease-causing factor" (see page 3, lines 21-27 of the

specification; emphasis added). The specification further notes that Applicant focused on the fact that cell death does not necessarily occur in all the cells contained in the affected area and that these "normal tissues" which do not develop pathological symptoms as well as tissues in the vicinity of the affected area may sufficiently express a disorder suppressor gene preventing the development of pathological symptoms (page 3, lines 27-36 and page 4, line 1). Therefore, at a minimum, it would appear the Applicant's invention is based on a concept that from the outset requires the use of *surviving or normal* cells present in or near an area of pathological cell death. Examiner notes that not one of the claims currently under examination recites the use of a cell or population of cells comprising "normal tissue or healthy cells" either present in an area showing cell death as a pathological feature, in the vicinity of such an area or otherwise. Moreover, based on Applicant's admission in the specification that the disease organs in subjects with disorders that accompany cell death usually may not be suitable objects for screening for disease suppressor genes, Applicant's inventive insight appears not to be the "general phenomenon" asserted in the remarks filed 12/12/2006.

Applicant's argument that in the instant case possession has been demonstrated by the recognition that 1) diseases involving cell death, including affected organs and tissues, were generally known as of the filing date; 2) neurodegenerative disorders, the affected tissues in such diseases and their characteristic clinical symptoms were also known in the art; and 3) procedures for making an expression library from a tissue sample were also well-known in the art at the time of Applicant's filing is not persuasive because those facts were not considerations upon which the written description rejection was made nor under which the instant claims are in dispute. The recited nucleic acids of the claims have been found to lack written description only insofar as they are "obtained from" or "synthesized from" those expressed in any "tissue of a nerve or brain" of any organism suffering from any neurodegenerative disorder of a cranial nervous system, "wherein said tissue is obtained from an area showing cell death as a pathological feature of the disorder" and further such that, so derived, a nucleic acid suppressor can be identified. As recited in the previous Office action, the demonstration that one nucleic acid sequence obtained from a pool of sequences present in the brain of an Alzheimer's disease patient, when expressed in F11 cells, leads to reduced cell death upon induction of V642I APP

expression is neither representative nor predictive of a method comprising the use of any other nucleic acid/nucleic acid library obtained from any other tissue showing cell death as a pathological feature. This would appear to be particularly true in light of Applicant's focus on a requirement for normal or resistant cells in the area of pathological cell death as well as Applicant's assertion that insight with regard to the presence of disorder suppressor genes in normal cells/tissue in or near the site of pathological cell death had not been previously described in the art (see page 9, lines 5-6 of the Remarks filed 12/12/06).

Examiner also finds Applicant's argument that a clearly defined process for obtaining nucleic acids is sufficient description of such nucleic acids unpersuasive. Applicant's argument that because one of ordinary skill in the art could carry out the process to obtain the nucleic acid library as recited in the claims, as well as a population of cells expressing the library, one of ordinary skill in the art would readily accept Applicant's possession of these features is not persuasive because it does not address all of the claimed features of Applicant's invention. These arguments are also unpersuasive because to the extent that they only address processes that were indeed well-known in the art, they are not

relevant to the rejection at hand. If Applicant's invention were limited to the attainment of a nucleic acid library and a population of cells expressing a library of nucleic acids, Applicant might indeed have provided written description support in the specification. However, Applicant's invention is drawn to a method of screening for a disorder suppressor gene from a library of nucleic acids obtained from any area showing pathological cell death as a feature of a neurodegenerative disorder of a cranial nervous system. As such, Applicant's invention encompasses the step of detecting a suppressive effect on said disorder due to the expression of a nucleic acid of the library and thereby identifying a suppressor gene of the disorder. Knowledge of existing neurodegenerative disorders of the cranial nervous system and procedures for making nucleic acid libraries, while required for practice of the invention, does not provide written description support for the use of any tissue of a nerve or brain from an area showing cell death as a pathological feature of said disorder, such that ultimately a disorder suppressor gene can be identified. Indeed, even in Applicant's working example(s), a suppression of cell death has only been observed in vitro, and the detection of a suppressive effect on Alzheimer's disease itself has not been tested. Furthermore, Applicant's method, based on Applicant's own

admission, is based on a concept which 1) requires the presence of normal or surviving tissue in an area of pathological cell death; 2) has not been previously described in the art; and 3) relies on normal or surviving tissue in the area of patholgocial cell death which "may" sufficiently express a disorder gene.

In light of such admissions, it is difficult to see how recitation of neurodegenerative diseases in the specification and/or consideration of the alleged well-accepted notion in the art that virtually all disorders are caused by a collapse in the balance between the action of disease-causing aberrant genes and disorder suppressor genes would lead one of ordinary skill in the art to conclude that Applicant was in possession of such a method as it applies to the use of any nerve or brain tissue from any area showing pathological cell death in any organism with a neurodegenerative disorder of the cranial nervous system. Furthermore, evidence need not be provided to refute the specification's disclosure or the knowledge in the art as summarized beyond those considerations which have already been set forth in the Office action mailed 7/11/2006 and the response to Applicant's remarks herein.

***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If

Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent applications to view

the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at (800) 786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

Walter A. Schlapkohl, Ph.D.
Patent Examiner
Art Unit 1636

February 22, 2007

DAVID GUZO
PRIMARY EXAMINER